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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/551,396

10/19/2006

Peter John Meikle

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EXAMINER

COUNTS, GARY W

ART UNIT

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09/27/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/551,396	Applicant(s) MEIKLE ET AL.	
	Examiner GARY W. COUNTS	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42,46,51-53 and 56-73 is/are pending in the application.
- 4a) Of the above claim(s) 1-41 and 58-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42,46,51-53,56 and 57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/31/10 & 09/10/10</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

The amendment filed 07/08/10 is acknowledged and has been entered. Currently, claims 1-42, 46, 51-53, and 56-73 are pending. Claims 1-41 and 58-73 are withdrawn as being directed to non-elected inventions. Claims 42, 46, 51-53, 56 and 57 are under examination.

Withdrawn Rejections

All rejections of claims not reiterated herein, have been withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 42, 46, 51-53, 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite “and a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney

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U (MWU) test". The specification on page 5, paragraph 0011 discloses that the ability to identify specific LSD enzymes in an automated multiplex assay will have a significant impact. The specification on page 33, paragraph 0105 discloses that figure 25 shows the Pearson correlation coefficient between each pair of target protein analytes. With the exception of A-iduronidase, the target antigens showed a significant correlation to the other antigens. The specification on pages 10-11, paragraph 0048 discloses that the pre-clinical status or the clinical status of an LSD can then be determined by comparing a deviation of the adjusted target quantity to the adjusted reference quantity. The specification on page 30, paragraph 0096 discloses that in contrast to absolute marker measurements, the multiplex allows each protein to be compared using ratios. For example, there was one four month old Pompe patient who had A-glucosidase blood spots levels in the lower range of the control group, this patient would have been missed in a typical screening program if the determined cut-offs used only absolute protein levels. There is no description in the specification disclosing a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test. Furthermore, none of the originally filed claims recited the limitations in question. Recitation of claim limitations lacking literal or adequate descriptive support in the specification or originally filed claims constitutes new matter.

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3. Claims 42, 46, 51-53, 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasma and dried blood samples obtained from a human, does not reasonably provide enablement for any and all biological samples or any and all target animals for determining a specific lysosomal storage disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re Wands* USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of detecting multiple Lysosomal Storage Disease ("LSD") target antigens in a sample, the protein profiling method comprising: (a) determining a target quantity of a-iduronidase or a-glucosidase from a target biological sample of a target animal; (b) determining a target quantity of either LAMP-1 or saposin from the target biological sample of the target animal; (c) assigning an adjusted target quantity by calculating a target proportion between the target quantity of a-iduronidase or a-glucosidase and the target quantity of either LAMP-1 or saposin C;

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(d) obtaining a reference quantity of a-iduronidase or a-glucosidase from a reference biological sample from a reference animal; or group of reference animals, having a known LSD pre-clinical or clinical status; (e) obtaining a reference quantity of either LAMP-1 or saposin C from the reference biological sample from a reference animal, or group of reference animals, having a known LSD pre-clinical or clinical status; (f) assigning an adjusted reference quantity by calculating a reference proportion between the reference quantity of a-iduronidase or a-glucosidase and the reference quantity of either LAMP-1 or saposin C; (g) determining a deviation of the adjusted target quantity compared to the adjusted reference quantity; and the determination of the target quantity of a-iduronidase or a-glucosidase,, the reference quantity of a-iduronidase or a-glucosidase, the target quantity of either LAMP-1 or saposin C, and the reference quantity of either LAMP-1 or saposin C are performed using a capture antibody conjugated to a microsphere, the microsphere having at least a first fluorophore and a second fluorophore, wherein the capture antibody is capable of binding to a-iduronidase or a-glucosidase or LAMP-1 or saposin C; and a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test.

The specification on page 13 discloses that the term “animal” refers to any species of the animal kingdom and in preferred embodiments refers more specifically to humans. The specification on page 1, paragraph 0003 discloses that LSDs represent a

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group of over 40 distinct genetic diseases that generally affect young children. Page 6 of the specification discloses determining the plasma concentrations from LSD individuals. Page 28 of the specification discloses plasma and blood samples were collected from infants, children and adults. The specification on pages 6-8 discloses determining LAMP-1, saposin C, a-glucosidase and a-iduronidase levels in plasma sample from individuals. The specification on page 28, paragraph 90 discloses that plasma samples and dried blood spots were used as example samples and discloses that other samples such as amniotic fluid, cellular extracts and urine may be used. However, the only working examples presented in the specification are directed to the detection of LAMP-1, saposin C, a-glucosidase and a-iduronidase antigen levels in plasma and blood samples and determining the levels of the antigens and determining lysosomal storage diseases. The specification does not show or provide guidance of obtaining a sample from any other subject than a human. For example, the specification does not provide samples taken from animals such as a cat, monkey, giraffe, dog etc. and determining levels of lysosomal storage disease antigens such as LAMP-1, saposin C, a-glucosidase and a-iduronidase and showing a correlation of the levels with an indication of a specific lysosomal storage disease. The specification also fails to provide guidance to a skilled artisan that the levels of the antigens in samples such as urine, amniotic fluid, cellular extracts, synovial fluid, cerebral spinal fluid, tears etc can be used to provide a pre-clinical or clinical indication of a specific lysosomal storage disease. Obrien et al., (The FASEB Journal, Vol 5, March 1991, pages 301-308) shows that the levels of saposins differ by body compartment in the case of brain,

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liver, and spleen (e.g. p. 307). Therefore, it can be expected that levels of saposins in another body compartment such as urine, spinal fluid or any other different biological sample would be similarly unpredictable. Therefore, one skilled in the art would not expect that the levels of antigens such as LAMP-1, saposin C, a-glucosidase and a-iduronidase would be consistent in any and all biological samples, or that the levels in such biological fluids would be correlated with an indication of a specific lysosomal storage disease.

Although the specification discloses a correlation between the levels of LAMP-1, saposin C, a-glucosidase and a-iduronidase in plasma and dried blood samples in humans with specific lysosomal storage diseases, there is not a disclosure of working examples of a correlation between the levels of the antigens in any other biological sample or in any other subject than that of a human. Therefore, for the reasons stated above it is not predictable that a correlation between the levels of the antigens in a biological sample such as urine, amniotic fluid or tears from a subject such as a horse, cat or dog provides an indication of a specific lysosomal storage disease in the subject. Thus, it would be undue experimentation for a skilled artisan to make and use the invention as claimed because there is not suggestion or guidance that a correlation of the levels of the antigens in any and all samples from any and all subjects is indicative of a specific lysosomal storage disease.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 42, 46, 51-53, 56 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42, lines 3-4 is vague and indefinite in reciting “a target biological sample” because it is unclear if Applicant is referring to the sample recited in line 2 or if Applicant intends another sample.

Claim 42, line 4 the recitation “the target animal” there is insufficient antecedent basis for this limitation.

Claim 42, line 6 the recitation “the target animal” there is insufficient antecedent basis for this limitation.

Claim 42 step (g) is vague and indefinite because it is unclear how the first and set fluorophores are related to detection. Also, the instant claims require the detection of multiple targets and it is unclear how one microsphere comprising only one antibody for a specific target is also able to detect the other targets in the assay. Is there more than one type of microsphere or more than one type of antibody? Therefore, it is unclear how the determination of the targets is made in the instantly recited claim.

Claim 46 is vague and indefinite in reciting the sample because it is unclear if Applicant is referring to the sample recited in line 2 of claim 42 or if Applicant is referring to the biological sample recited in line 4 of claim 42.

Response to Arguments

6. Applicant's arguments filed 07/08/10 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/
Examiner, Art Unit 1641

/Melanie Yu/
Primary Examiner, Art Unit 1641